Enhanced serum creatine kinase after neurosurgery in lateral position and intraoperative neurophysiological monitoring

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Abstract: OBJECTIVE: Several cases of highly elevated serum levels of creatine kinase (CK) after surgical interventions have been described in the literature. A consensus on possible risk factors is still lacking. We therefore studied CK-levels in a large population of patients undergoing neurosurgical interventions and sought to determine possible risk factors. METHODS: We retrospectively analyzed 150 elective neurosurgical interventions where pre- and postoperative CK serum levels were determined. The cases were selected such that 50 patients were operated in lateral position and 100 in prone or supine position. During the hospital stay, routine clinical diagnostics were conducted, including medical status and laboratory examinations. RESULTS: In the patient group (median age 50, 63 male) there were 129 cranial and 21 spinal interventions. In 55 cases, intraoperative neurophysiological monitoring (IONM) was performed so that in these patients muscles were not relaxed pharmacologically. In a linear regression model, the maximal postoperative CK-level increased compared to baseline ($p<0.001$). While age and obesity were not identified as risk factors, the CK-level was enhanced after surgery in lateral position ($p<0.001$) and if IONM was performed ($p=0.04$). CONCLUSIONS: The strong association of postoperative serum CK-level with intraoperative positioning and IONM may be related to the elevated body pressure on the operating table in the lateral position, in particular if muscles are not relaxed pharmacologically, which was the case if intraoperative monitoring was performed. In these cases special care has to be taken for the positioning and during the peri-operative management.

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Enhanced serum Creatine Kinase after neurosurgery in lateral position and intraoperative neurophysiological monitoring

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Keywords
creatine kinase, neurosurgery, lateral position, intraoperative neurophysiological monitoring, IONM

Objective

Several cases of highly elevated serum levels of creatine kinase (CK) after surgical interventions have been described in the literature. A consensus on possible risk factors is still lacking. We therefore studied CK-levels in a large population of patients undergoing neurosurgical interventions and sought to determine possible risk factors.

Methods

We retrospectively analyzed 150 elective neurosurgical interventions where pre- and postoperative CK serum levels were determined. The cases were selected such that 50 patients were operated in lateral position and 100 in prone or supine position. During the hospital stay, routine clinical diagnostics were conducted, including medical status and laboratory examinations.

Results

In the patient group (median age 50, 63 male) there were 129 cranial and 21 spinal interventions. In 55 cases, Intraoperative Neurophysiological Monitoring (IONM) was performed so that in these patients muscles were not relaxed pharmacologically. In a linear regression model, the maximal postoperative CK-level increased compared to baseline ($p<0.001$). While age and obesity were not identified as risk factors, the CK-level was enhanced after surgery in lateral position ($p<0.001$) and if IONM was performed ($p=0.04$).

Conclusions

The strong association of postoperative serum CK-level with intraoperative positioning and IONM may be related to the elevated body pressure on the operating table in the lateral position, in particular if muscles are not relaxed pharmacologically, which was the case if intraoperative monitoring was performed. In these cases special care has to be taken for the positioning and during the peri-operative management.

Introduction

Serum creatine kinase (CK) levels have served as a sensitive and valid marker of muscular injury in literature[1–8]. During prolonged surgery, diffuse local muscle compression with ischemia and subsequent reperfusion injury is inevitable, despite utilization of modern operating tables and padding[9,10]. Different manifestations after various surgical procedures ranging from simple serum CK rise to rhabdomyolysis with complex organ failure have been reported in literature[4,8,11–14]. With limited direct surgical trauma to the musculature during craniotomies, we hypothesize that postoperative CK excess is, among other factors, related to patient positioning. The purpose of the present study was to investigate a possible relationship between neurosurgical positioning and postoperative serum CK levels. This is, to our best knowledge, the first study investigating the effect of neurosurgical patient positioning on postoperative serum CK levels.

Patients and Methods

Patient inclusion criteria

In a retrospective study, we included neurosurgical patients who underwent elective craniotomy or spine surgery 2009-2011 and where repeated serum CK sampling was available. We included all patients where samples were available preoperatively and on both first and second postoperative day. With these criteria, patient records were retrospectively screened until three subgroups of 50 patients each were filled. The target group consisted of 50 craniotomies performed in the lateral position (Figure 2). Control groups consisted of patients operated in supine or prone position.

CK serum sampling

Total CK sampling was performed routinely without clinical signs, during pre and postoperative blood analysis by spectrometry using the Roche Modular System® (F. Hoffmann-La Roche Ltd Basel, Switzerland). Values were stored in the

patient records. The normal total CK levels as defined in our institution are in the ranges 25 - 190 U/L for men and 25 -167 U/L for women.

Intraoperative positioning and anesthesia

For patient positioning an ALPHAMAQUET 1150® operating table and additional devices were used (MAQUET AG, Gossau, Switzerland). General anesthesia was routinely performed by Total Intravenous Anesthesia (TIVA) using Propofol - Lipuro® (Disoprivan target-controlled-infusion, Braun Medical AG, Sempach, Switzerland), Fentanyl-Janssen® (Janssen-Cilag AG, Baar, Switzerland). If not stated otherwise, muscles were relaxed pharmacologically using Atracurium - Tracrium® (GlaxoSmithKline AG, Münchenbuchsee, Switzerland).

Intraoperative Neurophysiological Monitoring (IONM)

Depending on their localization, some surgical interventions required Intraoperative Neurophysiological Monitoring (IONM) (Figure 2). This includes the recording of compound muscle action potentials, which prohibits muscle relaxation. Therefore, in cases with IONM, the administration of Atracurium was stopped after intubation.

Data collection

Patient records were screened for the following values to be included in the analysis: preoperative CK level, a minimum of two postoperative CK levels, age at surgery, duration of surgery, body mass index (BMI), type of procedure (spinal or cranial), and positioning for surgery (lateral or prone or supine). Not all patients that underwent surgery had the required number of CK measurements. Therefore we do not have a consecutive case series. The omission of some patients did not introduce a selection bias since it occurred at random due to administrative reasons.

Statistical analysis

The preoperative measurement of the CK level was taken as baseline (CKpre). Among postoperative CK levels we included on the maximal level in further analysis (CKpost). All CK values were log-transformed to better comply with the assumptions of normality. The duration of surgery was transformed into a nominal variable (longer

or shorter than 4 hrs) as well as the BMI (below or above 25 kg/m2). We use linear regression to associate log(CKpost) to influencing variables and to adjust for confounders. Here it is necessary to include the value at baseline log(CKpre) as an influencing variable such that the results are corrected with respect to differences in baseline. Point estimates, confidence intervals (CI), and p-values are all likelihood-based. We use the significance level alpha = 0.05. All confidence intervals are computed at a confidence level of 95%.

Results

Patient and surgery characteristics

The patient group consisted of 63 male and 87 female patients with a median age of 50 years (range 15-81 years). The patients had a median BMI of 24.6 kg/m^2 (range 13.5-43.2 kg/m^2) and the BMI was below 25 kg/m^2 in 80 patients. The duration of surgery exceeded 4 hrs in 49 cases. There were 21 spinal and 129 cranial interventions. IONM was performed in a total of 55 surgeries, 30 of them in lateral position, indicating a highly significant association between IONM and lateral position (Fisher's Exact Test p<0.001).

Distribution and dependence of CK-levels

Preoperative routinely sampled CK levels (CKpre) ranged 0.5 – 3965 U/l (median 80 U/l) and the maximum of postoperative routinely sampled CK levels (CKpost) ranged 23 to 7066 U/l (median 191.5 U/l). In the distribution of CKpre there were three outliers, which had a strong leverage effect on all regression results; these three patients were excluded from further analysis. The values for CKpre and CKpost are depicted in Figure 1.

Table 1 shows the regression model of log(CKpost). The intercept shows that surgery alone leads to an average increase in log(CKpost) with respect to log(CKpre) by a factor of 1.24. Among all variables, CKpre hast the strongest influence on CKpost: An enhancement of log(CKpre) by one unit results in an average enhancement of log(CKpost) by 0.92, adjusted for all other variables. Furthermore, log(CKpost) is increased for a patient operated on in lateral position, adjusted for baseline and all other variables (p = 0.0009). Similarly, log(CKpost) is significantly increased if IONM is performed (p = 0.04). We did not find significant differences between spinal and

cranial interventions or long and short surgeries. Also age and BMI of the patients did not have a significant influence on the postoperative CK level.

Discussion

Our main findings

Our study revealed two important factors that increased CK serum levels: 1) we report that the postoperative CK level was significantly elevated after neurosurgical interventions if patients were operated on in lateral position ($p=0.0009$). 2) An additional raise occurred if IONM was performed ($p=0.04$). We attribute the effect of IONM not to IONM itself but rather to the fact absence of pharmacological relaxation during IONM.

Other factors like duration of surgical procedure, age and obesity could not be identified as statistically significant risk factors in our cohort. Furthermore, with limited muscular dissection during craniotomy, CK excess secondary to direct surgical trauma is unlikely.

Surgical positioning and CK levels

Among the factors investigated in our study, surgical positioning is the only one which can be influenced by the neurosurgeon. In neurosurgical interventions, the lateral position is mainly used for approaches to the posterior fossa, the brainstem and the skull base. It is known that several other surgical positions like lateral decubitus or extreme lithotomy position contribute to postoperatively elevated serum CK levels[4–6,9,15]. Anatomically abnormal positions expose the underlying musculature to higher pressure, leading to muscle ischemia and subsequent reperfusion injury after re-positioning[11]. Muscular injury is characterized by striated muscle cell necrosis and release of intracellular enzymes into the circulation, especially CK and myoglobin[1].

Other reasons for CK rise in the literature

Serum CK rise after various surgical procedures and even rhabdomyolysis has frequently been detailed reported in literature, especially after urological and bariatric operations[11–13,16–19]. There are several well-recognized risk factors for

muscular pressure injury and subsequent postoperative serum CK rise. Preoperative administration of steroids, statins as well as several neuromuscular blocking agents or the rare propofol infusion syndrome are known to cause muscle cell necrosis[2,20,21]. Loss of muscle tone due to administration of suxamethonium is known to facilitate ischemia and muscle cell necrosis[22]. However, in our study we observed an effect in the reverse direction as we found that absence of pharmacological muscle relaxation during IONM correlated with enhanced CK levels (p=0.04). There are also other factors that are discussed to lead to CK rise. While the influence of obesity remains controversial[3,14], super-obesity is regarded as major risk factor in literature[14,19]. However, neither obesity (BMI>25 kg/m2) nor super-obesity (BMI>30 kg/m2) showed influence on CK levels in our study. While one may think that the duration of surgical procedures might play a significant role, it did not in our study, being in line with the report by Arts and colleagues[3].

Consequences of enhanced CK levels

In our study we focus on the increase of CK levels irrespective of the normal range, since a large proportion of the patients had excess CK levels even before surgery (see Figure 1). Circulating muscle enzymes reflected by high CK levels may cause various complications, including acute renal, hepatic and respiratory failure[4,11–13]. These rare but serious conditions were never observed in our patient population. However, rhabdomyolysis in particular is not a clear-cut condition. Its clinical manifestations range from simple enzyme rise to life-threatening conditions[7]. With CK levels above 5000U/L, acute renal failure can occur[23]. Routinely CK sampling in the pre and postoperative course might be useful for screening patients with possible risk factors in this regard.

Consequences of our study

While positioning the patient for a neurosurgical procedure, care must be taken to avoid punctual muscular strain. Recently, Poli and colleagues related the absence of CK rise after prolonged treatment in intensive care units to specialized mattresses, which reduce pressure on muscles[8]. Improved padding and mattresses on the operating table may contribute to lower postoperative CK levels and subsequently decrease the risk of organ failure. Keller and colleagues

recently demonstrated in a randomized control trial that fluid mattresses are most effective in reducing interface pressure[10].

Conclusion:

The strong association of postoperative serum CK-level with intraoperative positioning may be related to the elevated body pressure on the operating table in the lateral position, in particular if muscles are not pharmacologically relaxed, which was the case if intraoperative monitoring was performed. In these cases special care has to be taken for the positioning and during peri-operative management.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Table 1: Regression model of log(CKpost). The variables CKpre, lateral position, and IONM have a significant influence on CKpost at a variable-wise significance level of alpha = 0.05.

	Estimate	p-value	95% confidence interval
Intercept	1.24	0.03	[0.12, 2.37]
log(CKpre)	0.92	>0.0001	[0.70, 1.13]
lateral position	0.62	0.0009	[0.26, 0.98]
IONM	0.37	0.04	[0.02, 0.72]
Spinal	0.32	0.16	[-0.13, 0.77]
OP duration > 4hrs	-0.22	0.22	[-0.57, 0.13]
Age	0.00	0.34	[-0.01, 0.01]
BMI>25 kg/m2	0.04	0.84	[-0.33, 0.41]
BMI>30 kg/m2	0.04	0.83	[-0.33, 0.41]

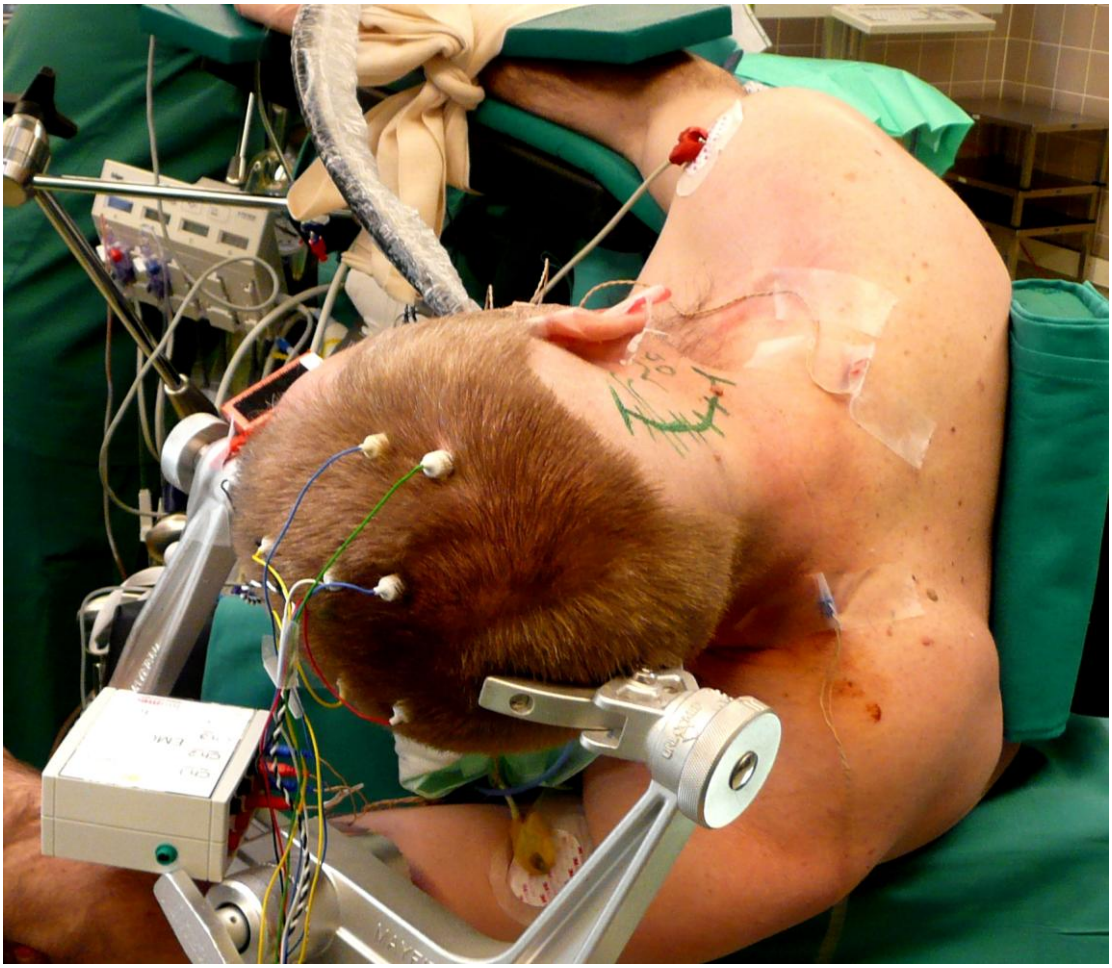

Figure 2: lateral positioning, with IONM and retrosigmoidal skin incision

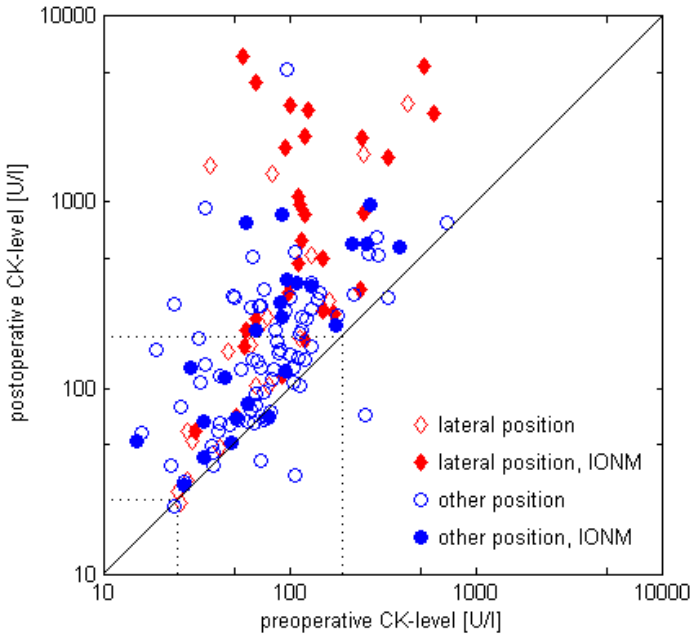

Figure 1: Enhanced serum CK level after neurosurgical interventions.

The preoperative CK level is plotted against the maximum of postoperative CK levels for each patient. Patients were operated on in lateral position (diamonds ◊), or in prone or supine position (circles ○). Filled symbols indicate that IONM was performed, which necessitates surgery without pharmacological muscle relaxation. The dotted lines delineate the normal range of CK levels.

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